GOLD STANDARD[SM] DIAGNOSTICS

K110899

FEB - 1 2012

510(k) Summary of Safety and Effectiveness

This 510(k) summary of safety and effectiveness information is being submitted in accordance with the requirement of SMDA 1990 and 21 CFR 807.92.

1) **Submitter's Name:** Gold Standard Diagnostics
   Address: 2851 Spafford St. Davis, CA. 95618
   Phone Number: 530-759-8000
   Contact Person: Napoleon Monce
   Date: September 20, 2011

2) **Product and Trade Name:**
   Helicobacter pylori IgA ELISA

   Common Name or Classification Name:
   Campylobacter pylori

   Product Code:
   LYR

3) **Legally marketed device to which the submitter claims equivalence:**
   Micro Detect, Inc. Pylori Detect IgA ELISA for the qualitative detection of IgA antibodies against *H. pylori* in human serum. The test is intended as an aid in the diagnosis of infection by *H. pylori* in patients with gastrointestinal symptoms. K003794.

4) **Description of the device:**
   The assay requires a total of 90 minutes incubation time. The test uses purified antigen coated on microtiter wells. Serum is added to each well and incubated for 30 minutes at 37°C. If *H. pylori* IgA antibodies are present they will bind to the antigen in the well. Unbound serum is removed by washing the wells three times. An HRP-conjugated anti-human IgA is then added to each well and incubated for 30 minutes at 37°C. If *H. pylori* antibody is present, it will bind to the antibody attached to the antigen on the well. The wells are again washed three times to remove any unbound conjugate. A TMB substrate is added to each well and incubated for 30 minutes at 37°C. If enzyme is present, it will react with the substrate to generate a colored product. After the incubation period, the reaction is stopped with a Stop Solution and the color intensity is measured spectrophotometrically.

5) **Intended use of the device:**
   The *Helicobacter pylori (H. pylori)* ELISA IgA test kit is intended for the qualitative detection of IgA antibodies to *H. pylori* in human serum in the adult population. This test is intended as a second test to aid in the diagnosis of *H. pylori* in patients with gastrointestinal symptoms, in conjunction with

clinical findings. It should be performed and interpreted with another assay for detection of IgG antibodies to *H. pylori.*

6) **Comparison with the predicate device:**
The Gold Standard Diagnostics *H. pylori* ELISA IgA Test Kit was compared to a commercially marketed kit by Micro Detect, Inc. the Pylori Detect IgA (K003794) catalog number HpKi-A. Both kits have the same intended use and use the same methodology. Below are tables comparing the reagents provided, the procedures, and their performances.

Table 1: Reagent Comparison

Gold Standard Diagnostics *H. pylori* ELISA IgA Test Kit	**Micro Detect Inc. Pylori Detect IgA**
Antigen coated Microtiter Plate – 96 wells	Antigen coated Microtiter Plate – 96 wells
Wash Solution – 20x	Diluent/Wash Concentrate – 25x
Diluent – Ready to Use	Diluent/Wash Concentrate – 25x
IgA Conjugate – Anti Human HRP	IgA Conjugate – Anti Human Peroxidase
Substrate – Tetramethylbenzidine (TMB)	Substrate – Tetramethylbenzidine (TMB)
Stop Solution – Acid mixture	Stop Solution – Sulfuric Acid
H. pylori IgA Positive Control	*H. pylori* IgA Positive Control
H. pylori IgA Cutoff Control	*H. pylori* IgA Calibrator
H. pylori IgA Negative Control	*H. pylori* IgA Negative Control

Table 2: Procedure Comparison

Gold Standard Diagnostics *H. pylori* ELISA IgA Test Kit	**Micro Detect Inc. Pylori Detect IgA**
Dilute Samples 1:101 in Diluent	Dilute Samples 1:101 in reconstituted Diluent/Wash
Add 100ul of Samples and Controls	Add 100ul of Samples and Controls
Incubate for 30 minutes at 37°C	Incubate for 20 minutes at Room Temperature

Wash four times with reconstituted Wash Solution	Wash three times with reconstituted Wash Solution
Add 100ul of Conjugate	Add 100ul of Conjugate
Incubate for 30 minutes at 37°C	Incubate for 20 minutes at Room Temperature
Wash four times with reconstituted Wash Solution	Wash three times with reconstituted Wash Solution
Add 100ul of Substrate	Add 100ul of Substrate
Incubate for 30 minutes at 37°C	Incubate for 15 minutes at Room Temperature
Add 50ul of Stop Solution	Add 100ul of Stop Solution
Read with Spectrophotometer at 450nm	Read with Spectrophotometer at 450nm

6(b1) Nonclinical tests:

The intra and inter assay precision was calculated by running six patient sera (four positives and two negatives) at three different sites. The results are summarized in the table below:

		Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6
Site 1	Ave:	0.945	0.803	0.860	0.498	0.091	0.115
	SD:	0.024	0.034	0.039	0.025	0.006	0.008
Intra-Assay	CV:	2.5%	4.2%	4.5%	5.0%	6.3%	7.1%
Site 2	Ave:	1.030	0.737	0.716	0.579	0.091	0.137
	SD:	0.060	0.057	0.041	0.046	0.004	0.009
Intra-Assay	CV:	5.9%	7.7%	5.7%	7.9%	4.8%	6.9%
Site 3	Ave:	0.996	0.667	0.768	0.579	0.091	0.151
	SD:	0.108	0.035	0.057	0.042	0.010	0.009
Intra-Assay	CV:	10.8%	5.3%	7.4%	7.3%	12.2%	6.1%
	Ave:	0.964	0.770	0.812	0.527	0.090	0.126
	SD:	0.062	0.063	0.074	0.049	0.007	0.017
Inter-Assay	CV:	6.4%	8.1%	9.1%	9.4%	7.4%	13.7%

Reproducibility:

The reproducibility of the assay was done by testing three samples in triplicate (a high negative, low positive and a moderate positive) for five days, twice a day, at three sites with two technicians per site. The results are summarized in the table below:

		5 Day Average:	Sample 1	Sample 2	Sample 3
Site 1	Tech 1	OD:	0.614	0.724	1.545
		SD:	0.045	0.066	0.091
		CV:	7.3%	9.1%	5.9%
	Tech 2	OD:	0.588	0.717	1.494
		SD:	0.059	0.073	0.091
		CV:	10.1%	10.2%	9.8%
Site 2	Tech 1	OD:	0.594	0.704	1.546
		SD:	0.034	0.045	0.082
		CV:	5.7%	6.4%	5.3%
	Tech 2	OD:	0.618	0.845	1.741
		SD:	0.036	0.044	0.071
		CV:	5.8%	5.2%	4.1%
Site 3	Tech 1	OD:	0.356	0.480	1.046
		SD:	0.048	0.087	0.128
		CV:	13.4%	18.0%	12.2%
	Tech 2	OD:	0.478	0.636	1.323
		SD:	0.086	0.110	0.148
		CV:	18.0%	17.3%	11.2%

Cross Reactivity:

An adsorption study was performed to evaluate any cross reactivity. Briefly, sera with different levels of antibodies to *H. pylori* were adsorbed with either *H. pylori*, *Candida albicans, E. coli, Borrelia burgdorferi, Clostridium* spp., *Campylobacter, Bacillus, Enterobacter, Pseudomonas, Haemophilus Influenza,* and *Proteus.* The identity of the bacteria used were identified by the ATCC and confirmed with mass spectrometry. The bacteria were evaluated at a concentration of 10^7 cfu/ml or higher.

Sera with different levels of antibodies to *H. pylori,* were adsorbed with the recommended organisms. The adsorbed samples were compared to the untreated samples and the mean percent inhibition was calculated. The results are summarized in the following table:

Organism	Concentration (cfu/ml)	Mean percent inhibition	Cross Reactivity
Helicobacter pylori		96%	
Candida albicans	2.40×10^7	0.8%	None

Escherichia coli	$6.90x10^7$	2.4%	None
Borrelia burgdorferi	$1.00x10^8$	4.3%	None
Clostridium spp.	$1.20x10^7$	1.7%	None
Campylobacter	$1.50x10^9$	3.3%	None
Bacillus	$4.40x10^7$	10.9%	None
Enterobacter	$1.80x10^8$	4.1%	None
Pseudomonas	$1.45x10^8$	3.8%	None
Haemophilus Influenza	$7.90x10^7$	5.8%	None
Proteus	$1.40x10^8$	3.1%	None

The mean percent inhibition for *H. pylori* was 96%, and 0.8% to 10.9% with the other organisms. Overall no effects on the analytical specificity were seen on the Gold Standard Diagnostics *H. pylori* ELISA IgA assay.

Interfering Substance

The effect of potential interfering substances on samples using the Gold Standard Diagnostics *H. pylori* ELISA IgA assay was evaluated. High levels of hemoglobin, bilirubin, cholesterol and triglycerides in serum samples were tested at the assay cutoff (9-11 units) in triplicate. The recommended concentrations from the guideline "Interference Testing In Clinical Chemistry" from the Clinical and Laboratory Standards Institute were used (see table below). No interference was noted with any of substances tested and the substances tested did not affect the performance of the Gold Standard Diagnostics *H. pylori* ELISA IgA assay.

Substance	**Concentration**	***H. pylori concentration***	**Mean Percent Inhibition**
Hemoglobin	2 g/L	9-11 units	9%
Bilirubin	342 µmol/L	9-11 units	7%
Cholesterol	13 mmol/L	9-11 units	0%
Triglyceride	37 mmol/L	9-11 units	-32%

Leukocytes, intestinal secretions or mucus, fat, and medications used to relieve diarrhea or other gastric symptoms were not tested, therefore, it is not known if these substances will interfere with the assay as they were not evaluated.

Limit of Detection

To determine the Limit of Detection (LoD) for the assay, a pooled positive and a pooled negative sample were tested along with the negative, cutoff and positive controls provided in the kit. Further, the pooled positive sample was diluted up to 4.3 fold. The samples, and dilutions, were then tested 24 times (24 replicates) over several days as described in the Clinical Laboratory Standards Institute CLSI document EP-17. The LoD chosen was one that gave a positive result 95% of the time, was near the cutoff, and gave acceptable precision and accuracy results.

In Summary, the controls supplied in the kit were within their acceptable ranges. The pooled negative sample gave negative results on all 24 replicates giving an average OD value of 0.050 and a corresponding Unit value of 1.1. The pooled positive sample gave positive results on all 24 replicates giving an average OD value of 1.259 and a corresponding Unit value 25.3.

The pooled positive sample was then diluted up to 4.3 fold and each dilution was tested with the assay. The 3.3 fold dilution was positive 95.8% of the time (after 24 replicates), gave acceptable precision and accuracy results, gave an average OD value of 0.558 was close to the average cutoff OD value (0.497) and gave a corresponding unit value of 11.3. Therefore, we can conclude that the LoD of the Gold Standard Diagnostics *H.* pylori IgA Test can be determined at an OD value of 0.558 and unit value of 11.3.

6(b2): Clinical Comparison:

The performance of the Gold Standard Diagnostics *H. pylori* ELISA IgA assay was determined by conducting a correlation study using 625 samples being routinely tested for H. pylori. The samples were tested on both the Gold Standard Diagnostics *H. pylori* ELISA IgA assay and a commercially available ELISA assay (Micro Detect Inc. K003794) as the predicate device. The results are summarized in the following table:

		Micro Detect Inc.		
		Positive	Equivocal	Negative
GSD	Positive	121	31	26
	Equivocal	13	8	23
	Negative	7	5	394

The discrepant samples were further tested on a third assay, the Inova QUANTA Lite™ *H. pylori* IgA ELISA (which is also commercially available). Of the seven Gold Standard Diagnostics negative samples, Micro Detect Inc. positive samples, the third assay called five samples positive. Of the 26 Gold Standard Diagnostics positive samples, Micro Detect Inc. negative samples, the third assay called two samples borderline, one sample negative and 23 samples positive.

The comparison data produced a percent positive agreement of 94.5% (C.I. 76.0% - 100%), a percent negative agreement of 93.8% (C.I. 88.8% - 99.5%), and an overall agreement of 94.0% (C.I. 85.9% - 100%).

6(b3) Conclusion:

From the data and comparison above, it is our contention that the Gold Standard Diagnostic *H. pylori* IgA ELISA test is substantially equivalent to the commercially marketed Micro Detect, Inc. Pylori Detect IgA kit.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

FEB - 1 2012

Gold Standard Diagnostics
C/o Napoleon Monce
Director, Product Development
2851 Spafford Street
Davis, CA 95618

Re: k110899
Trade/Device Name: Gold Standard Diagnostics Helicobacter pylori IgA Test Kit
Regulation Number: 21 CFR 866.3110
Regulation Name: Campylobacter fetus serological reagents
Regulatory Class: Class I
Product Code: LYR
Dated: January 18, 2012
Received: January 19, 2012

Dear Mr. Monce:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into class II (Special Controls), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice

requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): **K110899**

Device Name: **Gold Standard Diagnostics Helicobacter pylori ELISA IgA Test Kit**

Indications For Use:

The *Helicobacter pylori (H. pylori)* ELISA IgA test kit is intended for the qualitative detection of IgA antibodies to *H. pylori* in human serum in the adult population. This test is intended as a second test to aid in the diagnosis of *H. pylori* in patients with gastrointestinal symptoms, in conjunction with clinical findings. It should be performed and interpreted with another assay for detection of IgG antibodies to *H. pylori*.

Prescription Use X AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 807 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Freddie W. Poole
Division Sign-Off

Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K110899